C4 from a phage display library clone selected from the group consisting of pComb3/Fab(6) and pComb3/Fab(47).

REMARKS

Amendment

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

In The Specification

The specification has been amended to include SEQ ID Nos: on pages 25-26.

The 35 U.S.C. §112 Rejection

Claims 6, 12-14, 17-19 were rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. Applicants submit that the claimed biological materials are being deposited to obviate the

rejection and evidence of said deposit will be forwarded to the Examiner upon receipt.

Claims 6, 12-14, 17-19 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Applicants submit that the claimed biological materials are being deposited to obviate the rejection and evidence of said deposit will be forwarded to the Examiner upon receipt.

The 35 U.S.C. §102 Rejection

Claims 1, 3, 5 and 15 were rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent 5,686,600. The rejection is respectfully traversed.

Claim 1 is drawn to an antibody or an antibody fragment directed against the microvilli in the midgut region of a pest, wherein said antibody or antibody fragment is fused to a toxin. In contrast, the '600 patent teaches antibody directed against the brush border membrane vesicles of western corn rootworm. U.S. Patent 5,686,600 does not teach or suggest antibody directed against the microvilli in the midgut region of a pest as claimed herein. Neither does the '600 patent teach or suggest a method of using an antibody or an antibody fragment directed against the microvilli in the midgut region of a

pest. Since U.S. Patent 5,686,600 does not teach or suggest each and every aspect of the instant invention, the '600 patent does not anticipate claims 1 and 15 of the instant application. Accordingly, Applicants respectfully request that the rejection of claims 1, 3, 5 and 15 under 35 U.S.C. §102(e) be withdrawn.

The 35 U.S.C. §103 Rejection

Claims 1-5, 7-10 and 16 were rejected under 35 U.S.C. §103 as being unpatentable over U.S. Patent No. 5,686,600 in view of U.S. Patent No. 5,837,242 and U.S. Patent No. 5,870,852. This rejection is respectfully traversed.

The present invention discloses antibody compositions and methods of using these compositions to kill a pest such as fire ant. Claim 1 is drawn to a pest eradication product comprising a toxin fused to an antibody or fragment thereof directed against the midgut of a pest. Claim 7 is drawn to a pest eradication product comprising a first antibody or fragment thereof directed against the midgut of a pest, wherein said first antibody or fragment thereof is fused to a second antibody or fragment thereof directed against an antigenic epitope of a toxin.

In contrast, the '600 patent discloses the making of monoclonal antibodies that bind to gut antigens of corn rootworm and the use of these antibodies to kill corn rootworm. U.S. Patent No. 5,837,242 discloses the construction of multivalent or multispecific antibody fragments consisted of at least two polypeptide chains. The '852 patent teaches the use of hot water to kill fire ants. Applicants respectfully submit that combining the cited references does not lead a person having ordinary skill in this art to Applicants' claimed invention.

The Examiner contends that the instant invention differs from the prior art teachings by reciting specifically the killing of fire ant and one of ordinary skill in the art would have been motivated to use diabodies comprising scFv as taught by U.S. Patent No. 5,837,242 because diabodies are particularly useful in therapies as taught by U.S. Patent No. 5,837,242. Applicants respectfully disagree.

U.S. Patent No. 5,837,242 teaches the making of polypeptides containing one immunoglobulin heavy chain variable region and one immunoglobulin light chain variable region. These two variable regions on the same polypeptide are rendered incapable of associating with each other to form an antigen binding site. Two of

these polypeptides are dimerized to form "diabody" wherein the heavy chain variable region on one polypeptide associates with the light chain variable region on the other polypeptide to form an antigen binding site (abstract, column 2, line 60 to column 3, line 6 of U.S. Patent No. 5,837,242).

In contrast, the method of antibody generation and the structure of the antibody disclosed herein are both different and distinct from that of U.S. Patent No. 5,837,242. The present invention does not involve or require the use of diabodies as taught in U.S. Patent No. 5,837,242. Monoclonal antibodies or antigen fragments thereof of the present invention are derived from standard hybridoma techniques or phage display libraries. Generation of antibodies or fragments thereof for uses in the present invention does not require complex cloning and PCR steps to reshuffle the V-gene domains from scFv fragments as taught in U.S. Patent No. 5,837,242 (see column 28, lines 48-58; column 49, lines 11-15; column 50, line 23).

Moreover, the antibodies of the present invention are fused to other antibodies or a toxin molecule. This is in contrast to U.S. Patent No. 5,837,242 which describes "the design of bispecific

antibody fragments by taking advantage of the intermolecular pairing of VH and VL domains. This contrasts with the use of chemical crosslinking or fusion to dimerization peptides ..." (column 34, lines 39-47).

Therefore, the complicated teaching of genetic engineering for the generation of antigen binding fragments as taught in U.S. Patent No. 5,837,242 is irrelevant and not required for the present invention. The cited references do not teach or suggest a method of killing a pest by a toxin fused to an antibody or fragment thereof directed against the midgut of the pest. Neither does the combined teaching of the cited patents teach or suggest a method of killing a pest by an antibody composition comprising a first antibody or fragment thereof directed against the midgut of a pest fused to a second antibody or fragment thereof directed against an antigenic epitope of a toxin. The invention as a whole is not *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Accordingly, Applicants respectfully submit that the rejection of claims 1-5, 7-10 and 16 under 35 U.S.C. §103 be withdrawn.

This is intended to be a complete response to the Office Action mailed April 22, 2002. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

Date: Sept 23, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning on page 25, line 11 has been amended as follows:

cDNA synthesis RNA was isolated from mouse spleens (1/2 spleen from mice immunized with midgut preparations from imported fire ant queens as described in Example 1) using the guanidium isothiocyanate method. cDNA was prepared from 5 micrograms of RNA with oligo $(dT)_{16}$ as a primer. Reverse transcriptase, nucleotides, and buffers were purchased from PERKIN ELMER (RNA PCR Kit, Branchburg, New Jersey) and were used according to the instructions provided by the manufacturer. Fd and L chain cDNA were amplified by PCR. The 5' primers used were Light chain (GTGCCAGATGTGAGCTCGTGATGACCCAGTCTCCA, SEQ ID NO:1), V heavy chain a (AGGTCCAGCTGCTCGAGTCTGG, SEQ ID NO:2), VHb (AGGTCCAGCTGCTCGAGTCAGG, SEQ ID NO:3), V heavy chain c (AGGTCCAGCTTCTCGAGTCTGG, SEQ ID NO:4), and V heavy chain D (AGGTCCAGCTTCTCGAGTCAGG, SEQ ID NO:5) which introduced restriction sites (Sac I for light chains and XHO 1 for heavy chains) that facilitate their directional cloning into pComb 3. The 3' primers used were k chain (TCCTTCTAGATTACTAACACTCTCCCCTGTTGAA, SEQ

ID NO:6), C heavy 1 (AGGCTTACTAGTACAATCCCTGGGCACAAT, SEQ ID NO:7), thereby the k chain primer introduced an Xba 1 site and the heavy chain primer introduced a Spe 1 site. General conditions for PCR were Taq polymerase (Perkin Elmer, Branchburg, New Jersey) at 2.5 U/100-microliter reaction mixtures, 200 micromolar deoxynucleoside triphosphates, 1 millimolar $MgCl_2$, 5 microliters of cDNA per 100 microliters of reaction mixture, 150 ng of 5' primer and 150 ng of 3' primer in 1x buffer as supplied by the manufacturer (Perkin Elmer). Reaction mixtures were cycled at 94°C for 1.5 minutes, 52°C for 2.5 minutes, and 72°C for 3 minutes for a total of 40 cycles. These conditions have generated products of the correct size (660 bp) on all samples.

IN THE CLAIMS:

Claim 1 has been amended as follows:

1. (amended) A pest eradication product comprising:

~~a peptide~~ an antibody or an antibody fragment directed against the microvilli in the midgut region of a pest, wherein said antibody or antibody fragment is fused to a toxin. ~~an antigenic epitope of a gastrointestinal or digestive tract target cell of said pest; and~~

~~a toxin.~~

Claim 6 has been amended as follows:

6. (amended) The pest eradication product of claim 1, wherein said ~~peptide directed against said target cell antigen is an~~ antibody is secreted from a hybridoma selected from the group consisting of FA1, FA4, FA7, FA8, FA9, FA10, FA13, FA14, FA15, and FA17.

Claim 7 has been amended as follows:

7. (amended) A pest eradication product comprising:

~~a peptide~~ a first antibody or fragment thereof directed against the microvilli in the midgut region of a pest, wherein said first antibody or fragment thereof is fused to a second antibody or fragment thereof ~~an antigenic epitope of a gastrointestinal or digestive tract target cell of said pest~~;

~~a peptide~~ directed against an antigenic epitope of a toxin; ~~and~~

~~a toxin~~.

Claim 12 has been amended as follows:

12. (amended) The pest eradication product of claim 7, wherein said ~~peptide directed against said target cell antigen is an~~

antibody directed against said is secreted from a hybridoma selected from the group consisting of FA1, FA4, FA7, FA8, FA9, FA10, FA13, FA14, FA15, and FA17.

Claim 13 has been amended as follows:

13. (amended) The pest eradication product of claim 7, wherein said ~~peptide directed against said toxin is a n~~ antibody directed against said toxin is secreted from a hybridoma selected from the group consisting of G1, G2, G3, G4, G5, G6, and G7.

Claim 14 has been amended as follows:

14. (amended) The pest eradication product of claim 7, wherein said ~~peptide directed against said toxin is a n~~ antibody fragment directed against said toxin is derived from a phage display library clone selected from the group consisting of pComb3/Fab(6) and pComb3/Fab(47).